SECTION ON
CARDIOVASCULAR DISEASES

The Effects of Smoking on the Peripheral Circulation*

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We have been particularly interested in the problem of smoking on the peripheral vascular system of man. Because a man in good health may feel that smoking is bad only for one who is ill, information concerning the effect of smoking on normal individuals is important. Therefore, a total of 425 smoking tests was carried out on normal individuals. Because we wished to know also the effect of smoking tobacco on patients with peripheral vascular disease, further studies were carried out on such patients.

A standard smoking test has been devised. We expected little difficulty in determining the effect of smoking tobacco on the circulation of normal individuals. However, all methods of measuring peripheral blood flow in man are indirect, and certain factors that affect peripheral blood flow must be considered in order to obtain comparable measurements. Some of the confusion in the results of smoking tests has arisen because too little attention has been paid to (1) the environmental temperature, (2) the position of the subject, particularly of the extremities, (3) the taking of food, and (4) the basal metabolic rate.

The standard smoking test, as finally devised, used the skin temperatures as a measurement of blood flow. It took into consideration the four factors just listed and also required simultaneous observations of blood pressures, pulse rates and skin temperatures. The smokers inhaled with their accustomed depth and frequency during the 12 to 15 minutes required to smoke two thirds of two commercially available cigarettes.

The Normal Person

In an early study an attempt was made to determine how consistent were the results of the use of tobacco, whether a tolerance to smoking develops in habitual smokers and whether nicotine is the substance in smoke that causes the vascular effect. Sixty-six standard smoking tests were carried out on six normal subjects who were habitual smokers, four physicians and two women technicians whose basal metabolic rates ranged from −13 to +10 per cent. These studies showed that the responses to smoking of the skin temperature of the same individual varied from day to day according to the basal metabolic rate, but the increase of the blood pressure and pulse rate during smoking varied

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little from day to day. Thus, it became evident that the basal metabolic rate should be determined in each study with skin temperatures.

The skin temperature of the toes of all the subjects decreased an average of 2.5° C. (4.5° F.) with a range from 1° to 4° C. (1.8° to 7.2° F.) during smoking. For the fingers the average decrease was 3.2° C. (5.8° F.). The average increase of blood pressure during smoking was 20 mm. of mercury systolic and 14 mm. diastolic. The pulse rate increased an average of 36 beats per minute; the range was from 20 to 52 beats. The electrocardiographic changes consisted of increased heart rate, decreased amplitude of T waves and inverted T waves in one instance.

Habitual smokers did not show tolerance to the effects of smoking as the skin temperatures of the extremities decreased and the blood pressure and pulse rate increased. The decrease of the skin temperature was not related to the length of time the subject had been a smoker or the number of cigarettes smoked a day.

Several groups of additional tests were necessary to determine whether the vascular changes were due to nicotine and how much the content of nicotine had to be decreased to banish the vascular effects. Normal subjects were given a solution of sodium chloride intravenously as a control, and then 2 mg. of nicotine was added to the solution without the subjects' knowing when it was added. The skin temperatures of these persons decreased rapidly and definitely, the heart rate increased,
and the amplitude of the T waves in the electrocardiographic tracing decreased with administration of nicotine.

The second group of tests consisted of 30 smoking tests with various commercially available denicotinized cigarettes. The vascular effects were similar to those obtained when standard cigarettes were smoked.

To determine how much the content of nicotine in a cigarette should be decreased to banish the vascular effects of smoking, 192 standard smoking tests were done on 29 normal subjects who were between 20 and 36 years of age. Six different batches of cigarettes were used. The main stream of smoke from one cigarette of each batch contained respectively an average of 0.23, 0.55, 1.28, 1.83, 2.47 and 3 mg. of nicotine. As the concentration of nicotine in the main stream of the smoke was increased, the skin temperatures of both the fingers and toes decreased until the effects were the same as those from standard cigarettes (Fig. 1). The lower the concentration of nicotine in the smoke the less the blood pressure and pulse rate increased (Fig. 2) from the basal level and vice versa. The increase was sharp when the concentration of nicotine was raised from 0.55 to 1.28 mg. This study indicated that nicotine is responsible for the vascular changes which accompany smoking, and these observations explain why the same vascular effects were obtained during the smoking of standard cigarettes and denicotinized cigarettes. Apparently, the content of nicotine in a cigarette must be decreased more

![Figure 2: Effect on the skin temperature of the toes and fingers caused by smoking two cigarettes, the main stream of the smoke of which contained various concentrations of nicotine. Observations of the effects of each concentration of nicotine were divided into three groups, A, B and C, according to the basal heat production. As compared with the fingers, the decrease in skin temperature of the toes was less, particularly in groups A and B, irrespective of the concentration of nicotine. Also, as the concentration of nicotine was increased, the decrease of the skin temperatures became greater.](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21336/)
than 60 per cent from that in a standard cigarette before smoking produces only slight or no vascular effects.

The normal person often feels that alcohol will inhibit the vascular effects of smoking since the oral administration of alcohol dilates the blood vessels of the extremities. To study this problem we carried out smoking tests in the usual way and on the next day we investigated the effect of smoking after the taking of alcohol on the same persons. To do this we carried out 87 smoking tests after the ingestion of 1 ounce of 95 per cent alcohol in fruit juice. Smoking began between 30 and 60 minutes after the ingestion of the alcohol at the height of the vasodilatation as measured by the increase in the skin temperature. The blood pressure and pulse rate rose definitely on smoking after the ingestion of alcohol. The skin temperature of the fingers and toes decreased below the basal level on smoking after ingestion of alcohol in 72 per cent of the subjects. Alcohol in this study did not prevent vasoconstriction from smoking.

In the normal person, then, tolerance does not develop to tobacco so far as the vascular effects are concerned; the blood pressure and pulse rate increase and the skin temperature of the extremities decreases on smoking tobacco; nicotine appears to be the most important factor in producing the vascular effects, and alcohol does not nullify the effect of smoking.

Effect in Peripheral Vascular Disease

The effects of smoking on patients with peripheral vascular disease as determined by the smoking test are a significant fall in the skin temperatures of the fingers and toes and a rise in blood pressure and pulse rate. The variations are similar to those of normal subjects and most likely are in association with the basal metabolic rate.

The evidence that smoking plays a role in the progression of peripheral vascular disease is no longer controversial. Although it may not be the etiologic factor, it is certainly the most prominent contributing factor. A nonsmoker rarely, if ever, is seen with thromboangiitis obliterans at the Mayo Clinic, and various reports have been made of the relief of symptoms after cessation of smoking.

In view of this, the discussion of filters and filtered cigarettes produced as a protection in removing nicotine and tars from cigarette smoke is highly important. We found that the vascular effects were the same for filtered cigarettes as for nonfiltered cigarettes. The Chemical Laboratory of the American Medical Association has reported that the fraction of nicotine removed from the main stream of the smoke by the filter is small. To avoid the vascular effects, such efficient filters could be made that the culminating achievement would be a filter that would pass no smoke at all. It is exceedingly doubtful that the average smoker would take kindly to this.

Wright did not find any filtered cigarettes that did not produce a response in the vascular system. In addition, he repeatedly observed relapse in thromboangiitis obliterans when patients smoked filtered cigarettes. He described a patient who first had active thromboangiitis obliterans in 1940. On stopping smoking, his symptoms remained quiescent until 1949 when he resumed smoking. In 6 months gangrene of
three toes developed. Once more, on abstinence from smoking the disease became quiescent. Four months after beginning to smoke filtered cigarettes, his disease has been reactivated, and he has early pregangrenous involvement of two toes.

Mediation of the Vasoconstriction Due to Smoking

Earlier workers attributed the vasoconstriction of the peripheral blood vessels by smoking to stimulation of the sympathetic nervous system and questioned whether the absorbed nicotine caused the whole effect. Rapaport, Frank and Massell reported that lumbar sympathectomy abolished the peripheral vasoconstriction produced by smoking in the lower extremities of 19 patients. They concluded that the vasoconstriction, therefore, is mediated by sympathetic vasomotor fibers and not by humoral agents such as epinephrine or posterior pituitary hormone. We also have found (Fig. 3) no vasoconstriction as indicated by a decrease in the skin temperature of the toes during smoking if lumbar sympathectomy was complete, but smoking decreased the skin temperatures of the fingers. Thus after lumbar sympathectomy the intact sympathetic nervous system seems to function in a more than adequate manner.

FIGURE 3: Effect of smoking on the fingers and toes after extensive lumbar sympathectomy. Reversal of temperatures of the fingers and toes, with no effect of smoking on the temperatures of the toes but a mild fall on temperatures of the fingers, should be noted.
Schminterlow in 1948 showed that norepinephrine is present in the wall of the peripheral arteries. Halmovici reported from profusion experiments in animals that nicotine may act directly on the blood vessels because the vasoconstrictor action of nicotine occurred even after the removal of the sympathetic chains and of the spinal nerves. According to Burn and Rand this vasoconstriction in the rabbit is due to the release of norepinephrine from the wall of the arteries. Several workers have presented evidence for and against the theory that smoking increases the secretion of epinephrine and norepinephrine with a subsequent elevation in the blood sugar.

With newer methods available, Rehder and one of us (Roth) attempted to determine whether smoking of tobacco increased the production of epinephrine and norepinephrine in man and in turn increased the blood sugar. We carried out smoking tests on 24 normal subjects under basal conditions. During the control period blood was drawn through a siliconized needle for blood sugars determined by the Somogyi and Nelson method and epinephrine-like substances determined by the method of Weil-Malherbe and Bone. Skin temperatures, blood pressure and pulse rates were measured at 10-minute intervals. Blood was drawn for determination of blood sugar at intervals of 3, 5, 10 and 15 minutes after smoking was begun and for pressor amines between 3 and 5 minutes after smoking was begun. We measured the skin temperature, blood pressure and pulse rate at 1-minute intervals during smoking. The levels of the fasting blood sugar and the epinephrine-like substances of the systemic blood did not rise appreciably. However, a definite stimulation of the sympathetic nervous system occurred as evidenced by the significant rise of the pulse rate and blood pressure and the decrease of the skin temperatures of the fingers and toes.

**SUMMARY**

Because a man in good health may feel that smoking is bad only for one who is ill, information concerning the effect of smoking on normal individuals is important. Therefore, a total of 425 smoking tests was carried out on 100 normal individuals.

The standard smoking test, as finally devised, used the skin temperatures as a measurement of blood flow together with measurements of blood pressure and pulse rate.

Our studies disclosed that on the normal person tolerance does not develop to tobacco so far as the vascular effects are concerned; the blood pressure and pulse rate increase and the skin temperature of the extremities decreases on smoking tobacco; nicotine appears to be the most important factor in producing the vascular effects, and alcohol does not nullify the effect of smoking.

The effects of smoking on patients with peripheral vascular disease as determined by the smoking test are similar to those of normal subjects and most likely are in association with the basal metabolic rate.

The evidence that smoking plays a role in the progression of peripheral vascular disease is no longer controversial.

We found no vasoconstriction as indicated by a decrease in the skin temperature of the toes during smoking when lumbar sympathectomy was complete, but smoking decreased the skin temperatures of the fingers.

Rehder and Roth found also that the levels of the fasting blood sugar and the epinephrine-like substances of the systemic blood did not rise appreciably with smoking.

**RESUMEN**

Puesto que un hombre en buen estado de salud puede creer que el fumar sólo es dañoso para los enfermos, es importante el estudio de los efectos del fumar en los sujetos normales.

Por tanto, se hicieron 425 pruebas de fumar en individuos normales y más estudios se hicieron en enfermos con enfermedad vascular periférica.
La prueba estandar del fumar como finalmente se ideó, fue la medida de las temperaturas cutáneas como reveladora del flujo sanguíneo.

Nuestros estudios descubrieron que en las personas normales no desarrollan tolerancia al tabaco en lo que se refiere a los efectos vasculares; la presión sanguínea y la frecuencia del pulmón aumentan y la temperatura cutánea de las extremidades, decrece al fumar tabaco; la nicotina parece ser el factor más importante para producir los efectos vasculares y el alcohol no neutraliza los efectos del tabaco.

Los efectos del fumar en los enfermos vasculares periféricos según se ha determinado por estas pruebas, son similares a los que se observan en los sujetos normales y muy probablemente se asocian con los cambios del metabolismo basal.

Ya no se presta a controversia la evidencia que el fumar desempeña un papel en la evolución de la enfermedad vascular periférica.

No encontramos vasoconstricción según lo indica el decrecimiento de la temperatura de la piel en los dedos gordos del pie durante el fumar cuando la sympathectomía lumbar era completa, pero el fumar hacía decrecer la temperatura de los dedos de la mano.

Rehder and Roth también encontraron que los niveles de la glucemia en ayunas y las substancias similares a la epinefrina en la sangre de la circulación mayor no subieron notablemente al fumar.

RESUMÉ

Parce qu'un homme en bonne santé peut penser que fumer n'est mauvais que pour celui qui est malade, il est important de donner des renseignements sur l'effet de la fumée sur des individus normaux. C'est pourquoi les auteurs ont pratiqué 425 tests à la fumée chez des individus normaux, et des études ultérieures furent pratiquées sur des malades atteints d'affections vasculaires périphériques.

Le test standard à la fumée, selon sa dernière mise au point, utilise les températures cutanées comme mesure du débit sanguin.

Nos études révèlèrent que chez l'individu normal, l'intolérance au tabac ne se développe pas tant que les effets vasculaires ne sont pas perceptibles; la pression sanguine et le pouls augmentent et la température cutanée des extrémités décroît à l'occasion de la fumée; la nicotine semble être le facteur le plus important dans la production des effets vasculaires, et l'alcool n'annule pas l'effet de la fumée.

Les effets de la fumée sur les malades atteints d'affections vasculaire périphérique, selon ce qui a été déterminé le test, sont semblables à ceux produits chez les sujets normaux et sont plus vraisemblablement en association avec le taux du métabolisme basal.

L'évidence selon laquelle la fumée joue un rôle dans la progression de l'affection vasculaire périphérique n'est plus controversée.

Nous n'avons pas trouvé de vasoconstriction qu'aurait indiqué la diminution de la température cutanée des orteils pendant que l'individu fume lorsqu'il avait subi une sympathectomie lombar complète, mais la fumée fit décroître les températures cutanées des doigts.

REHDER et ROTH trouvèrent également que le taux du sucre sanguin et des substances de la circulation générale voisines de l'adrénaline ne s'élevait pas considérablement avec la fumée.

ZUSAMMENFASSUNG


Der Standard-Rauchtest, wie er schliesälisch ausgedacht wurde, machte Gerbrauch von der Hauttemperatur als Mass der Durchblutung. Unsere Untersuchungen erwiesen, dass sich bei normalen Personen so welt keine Tabak-Verträglichkeit entwickelt, wie es die Gefässwirkungen angeht; Blutdruck und Pulsfrequenz nehmen zu, und die Hauttemperatur der Extremitäten nimmt beim Rauchen von Tabak ab; Nikotin scheint der wichtigste Faktor zu sein für das Zustandekommen der Gefässdefekte, und der Alkohol hebt die Wirkung des Rauchens durchaus nicht auf.


Das Beweismaterial, wonach das Rauchen eine Rolle spielt für die Progredienza peripherer Gefässerkrankung, ist nicht länger umstritten.

Wir fanden keine Vasokonstriktion, wie sie bemerkbar wird an einer Abnahme der Hauttemperatur der Zehen während des Rauchens, wenn eine komplette, lumbale Sympathektomie vorlag; aber das Rauchen setzte die Hauttemperatur der Finger herab.

Rehder und Roth fanden ausserdem, dass der Nüchten-Blutzucker-Spiegel und derjenige von epinephrinartigen Substanzen im grossen Kreislauf beim Rauchen nicht messbar anstieg.
REFERENCES


